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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,576	12/01/2003	Kirill Ostanin	60409CON(50370)	9888

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EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 07/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/729,576	OSTANIN ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-42* is/are pending in the application.

4a) Of the above claim(s) *39-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6, 9-11, 14, 16-20, 23-25, 35-38* is/are rejected.

7)☒ Claim(s) *7,8,12,13,15,21,22 and 26-34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' amendment filed on 05/2/2006 has been entered. Claims 1, 10, 19, have been amended. Claims 1-4 and 6-42 are pending. Claims 1-4 and 6-38 are under consideration. Claims 39-42 are withdrawn from consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Withdrawn Objections and/or Rejections

The rejection of claim 19 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of amended claim.

The rejection of claims 1-4, 35, and 38 under 35 U.S.C. 102(e) as being anticipated by Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) has been withdrawn in view of amended claims.

The rejection of claim 5 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705) in view of Cappellaro et al. (EMBO J. 10 :4081-4088, 1991) has been made moot by cancelled claim.

The rejection of claims 6, 9-11, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed

on September 24, 1997) in view of Alberts et al. (Molecular Biology of the Cell, 2nd Edition, Garland Publishing, Inc, 1989) has been withdrawn in view of amended claim 1, from which claims 6, 9-11, and 14 depend.

The rejection of claims 7 and 8 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Alberts et al. (Molecular Biology of the Cell, 2nd Edition, Garland Publishing, Inc, 1989), and further in view of Wojciechowicz et al (Mol. Cell. Biol. 13:2554-2563, 1993) has been withdrawn in view of amended claim 1, from which claims 7 and 8 depend.

The rejection of claims 12 and 13 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Cappellaro et al. (EMBO J. 10 :4081-4088, 1991), and further in view of Wojciechowicz et al (Mol. Cell. Biol. 13:2554-2563, 1993) has been withdrawn in view of Applicants' argument.

The rejection of claim 15 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of both Cappellaro et al. (EMBO J. 10:4081-4088, 1991) and Wojciechowicz et al. (Mol. Cell. Biol. 13:2554-2563, 1993), and further in view of Wu et al. (Analytical Biochemistry, 249:29-36, 1997) has been withdrawn in view of Applicants' argument.

The rejection of claims 21 and 22 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Cappellaro et al. (EMBO J. 10:4081-4088, 1991) and Alberts et al. (Molecular Biology of the Cell, 2nd Edition, Garland Publishing, Inc, 1989) and Nare et al. (Analytical Biochemistry, 267:390-396, 1999), and further in view of Wojciechowicz et al (Mol. Cell. Biol. 13:2554-2563, 1993) has been withdrawn in view of Applicants' argument.

The rejection of claim 26 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Roy et al. (Mol. Cell. Biol. 11:4196-4206, 1991) has been withdrawn in view of Applicants' argument.

The rejection of claims 27-29 and 32-34 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Roy et al. (Mol. Cell. Biol. 11:4196-4206, 1991), and further in view of both Alberts et al. (Molecular Biology of the Cell, 2nd Edition, Garland Publishing, Inc, 1989) and Nare et al. (Analytical Biochemistry, 267:390-396, 1999) has been withdrawn in view of Applicants' argument.

The rejection of claims 30 and 31 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of both Roy et al. (Mol. Cell. Biol. 11:4196-4206, 1991), Alberts et al.

(Molecular Biology of the Cell, 2nd Edition, Garland Publishing, Inc, 1989), and Nare et al. (Analytical Biochemistry, 267:390-396, 1999), and further in view of Wojciechowicz et al (Mol. Cell. Biol. 13:2554-2563, 1993) has been withdrawn in view of Applicants' argument.

The rejection of claims 36 and 37 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Reppert (U.S. Patent No. 6037,131, March 14, 2000, filed on March 29, 1999) has been withdrawn in view of amended claim 1, from which claims 7 and 8 indirectly depend.

The objection of claims 36 and 37 are withdrawn.

Claim Rejections Under 35 U. S. C. §112, the 2nd paragraph

The rejection of claims 9 and 10 under 35 U.S.C. 112, second paragraph, is maintained.

Applicants argue that the cell recited in claim 1 is incubated with detector molecule conjugated with a reporter moiety and that claim 9 recites that the reporter moiety is a reported gene, whereas the term "reporter gene" is defined in the instant application. This is not persuasive because according to the context of claim 6, "incubating said cell with a substrate appropriate for said reporter moiety", the term "reporter gene" recited in claims 9 and 10 should be "reporter", i.e., a protein product of reporter gene. It is also

noted that claim 10 recites the limitation "reporter gene" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections Under 35 U. S. C. § 103(a)

(i). The rejection of claims 11, 14, 16, and 17 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Cappellaro et al. (EMBO J. 10 :4081-4088, 1991) is maintained. Amended claims 1-4, 35, and 38, are also rejected on the same basis.

Claims 1-4, 11, 14, 16, 17, 35, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Cappellaro et al. (EMBO J. 10 :4081-4088, 1991).

Trueheart et al. teach an assay for identifying a compound that modulates a heterologous receptor that is functionally integrated into an endogenous yeast pheromone response pathway (See, Claims 1 and 2). Tureheart teach that the cells used in the assay can be any type of cells, including yeast cells or MATa *Saccharomyces cerevisiae* cells (Column 2, 4th paragraph; Column 13, line 4; Column 15, last two paragraphs). Trueheart et al. further teach a G-protein coupled receptor (C5a receptor) functionally coupled to the endogenous yeast GPA-1 protein subunit (Column 61, example 4).

Trueheart et al. fail to teach (1) the use of the protein product of AGA2 gene (a-agglutinin) as a detectable signal (re: claim 1); (2) a detector molecule conjugated with a reporter moiety (re: claims 11 and 14); or (3) an extraction step comprising treatment of the cells with a reducing agent (re: claims 16 and 17).

Cappellaro et al. teach the characterization of AGA2 gene and protein, as well as the interaction of the protein product of AGA2 gene (a-agglutinin) with α-agglutinin (See the whole document). Cappellaro et al. also teach staining of yeast cells to detect a-agglutinin with an anti-a-agglutinin antibody labelled with FITC (page 4087, last paragraph-page 4088, 1st paragraph). Cappellaro et al. further teach extraction of a-agglutinin from MATa *S. cerevisiae* yeast cells by treating the cells with a reducing agent, dithiothreitol (page 4081, right column, 3rd paragraph).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include (1) the use of the protein product of AGA2 gene (a-agglutinin) as a detectable signal; (2) the use of an anti-a-agglutinin antibody labelled with FITC for the detection of a-agglutinin; or (3) the extraction step comprising treatment of the cells with a reducing agent in the method taught by Trueheart et al. with a reasonable expectation of success. One skilled in the art would have been motivate to do so because (1) activation of pheromone response pathway induces production of the protein product of AGA2 gene (a-agglutinin) that specifically reacts with and binds to α-agglutinin (page 4082, right column, 5th paragraph), (2) treatment of the cells with a reducing agent results in release the cell surface signal molecules (such as a-

agglutinin), and (3) an fluorescing antibody offers a sensitive means for the detection of a signal, as taught by Cappellaro et al.

Response to Applicants' argument

Beginning at the bottom of page 9 of Applicants' reply filed on 05/22/2206, Applicants argue that Applicants were the first to appreciate that the protein product of an AGA2 gene could be used as a read-out for compound screening. Applicants argue that Trueheart fails to recognize that AGA2 protein could be used in compound screening methods. There is no express teaching or suggestion that the assay of True heart should be modified to include the use of AGA2 as a readout.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the rejection is a 103(a) rejection. Claims 1-4, 11, 14, 16, 17, 35, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705) in view of Cappellaro et al. (EMBO J. 10 :4081-4088, 1991). Applicants cannot only criticize one reference alone.

Beginning at the middle of page 11 of Applicants' reply filed on 05/22/2206, Applicants argue that Capellaro merely characterizes the active domain of AGA2. Capellaro plainly fails to teach or suggest any method of compound screening, much less adapting the compound screening methods described by Trueheart by employing the AGA2 protein product as a readout.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the rejection is a 103(a) and is based upon the combined teachings of Trueheart et al. and Cappellaro et al. Criticizing one prior art is not sufficient to overcome the rejection.

At the 2nd paragraph of page 12 of Applicants' reply filed on 05/22/2206, Applicants argue that there is nothing in Trueheart suggesting a problem with the screening assays disclosed therein such that one of ordinary skill in the art would be motivated to seek an alternative signalling paradigm. Applicants also argue that because Cappellaro is silent as to screening assays and because there is nothing in Trueheart that would motivate one of ordinary skill in the art to seek a read out other than those disclosed in Trueheart, one of ordinary skill in the art would not be motivated to combine the references as suggested by the Examiner.

Applicants' argument has been fully considered, but is not deemed to be persuasive because in view of the combined teachings of Trueheart et al. and Cappellaro et al., it would have been obvious to one having ordinary skill in the art at the time the invention was made to include (1) the use of the protein product of AGA2 gene (a-agglutinin) as a detectable signal; (2) the use of an anti-a-agglutinin antibody labelled with FITC for the detection of a-agglutinin; or (3) the extraction step comprising treatment of the cells with a reducing agent in the method taught by Trueheart et al. with a reasonable expectation of success. An artisan would have been motivate to do so because (1) activation of

pheromone response pathway induces production of the protein product of AGA2 gene (a-agglutinin) that specifically reacts with and binds to α-agglutinin (page 4082, right column, 5th paragraph), (2) treatment of the cells with a reducing agent results in release the cell surface signal molecules (such as a-agglutinin), and (3) an fluorescing antibody offers a sensitive means for the detection of a signal, as taught by Cappellaro et al.

(ii). Claims 6, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Cappellaro et al. (EMBO J. 10: 4081-4088, 1991), as applied to claims 1-4, 11, 14, 16, 17, 35, and 38, and further in view of Alberts et al. (Molecular Biology of the Cell, 2nd Edition, Garland Publishing, Inc, 1989).

Trueheart et al. and Cappellaro et al. teach a method for identifying a compound that modulates a heterologous receptor in a cell, as applied to claims 1-4, 11, 14, 16, 17, 35, and 38 above.

Trueheart et al. and Cappellaro et al. fail to teach a detector molecule conjugated with a reporter moiety as recited in the claims.

However, use of a detector molecule conjugated with a reporter moiety is well known in the art. For example, Alberts et al. teach the use of antibodies coupled with a marker

molecule (a reporter) for detecting specific molecules in cells (page 177; page 178, Figure 4-58). Alberts also teach the use of a fluorescent dye and an enzyme (alkaline phosphatase, horseradish peroxidase) (page 177; page 178, Figure 4-58).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include a detector molecule conjugated with a reporter moiety in the method taught by Trueheart et al. and Cappellaro et al. with a reasonable expectation of success. The motivation to do so would have been to develop the most sensitive method using an antibody conjugated with a reporter moiety, as taught by Alberts et al. (pages 177-178).

(iii). The rejection of claims 18-20 and 23-25 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Cappellaro et al. (EMBO J. 10 :4081-4088, 1991), and further in view of both Alberts et al. (Molecular Biology of the Cell, 2nd Edition, Garland Publishing, Inc, 1989) and Nare et al. (Analytical Biochemistry, 267:390-396, 1999) is maintained.

(iv). Claims 36 and 37 under 35 U.S.C. 103(a) as being unpatentable over Trueheart et al. (U.S. Patent No: 6159705, December 12, 2000, filed on September 24, 1997) in view of Cappellaro et al. (EMBO J. 10: 4081-4088, 1991), as applied to claims 1-4, 11, 14,

16, 17, 35, and 38, and further in view of Reppert (U.S. Patent No. 6037,131, March 14, 2000, filed on March 29, 1999).

Trueheart et al. and Cappellaro et al. teach a method for identifying a compound that modulates a heterologous receptor in a cell, as applied to claims 1-4, 11, 14, 16, 17, 35, and 38 above.

Trueheart et al. and Cappellaro et al. fail to teach the use of melatonin 1a receptor and other heterologous receptors listed in claim 36. However, all the receptors listed in claim 36 have been cloned and well characterized. For example, Reppert teaches expression of melatonin 1a receptor gene in mammalian cells (Column 7, Example 2).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include melatonin 1a receptor of Reppert in the method taught by Trueheart et al. and Cappellaro et al. with a reasonable expectation of success. One skilled in the art would be motivated to do so because melatonin 1a receptor has important biological functions.

Response to Applicants' argument

Beginning at page 14 of Applicants' reply filed on 05/22/2206, Applicants argue that the cited references of Alberts, Nare and Reppert uniformly lack even the most tenuous connection with the claimed methods and that the references of Alberts, Nare and

Reppert are cited merely because they allegedly describe elements present in Application claims. Applicants submit that the recitation of such disparate elements of the claims is insufficient to establish obviousness with respect to these references. This has been fully considered, but is not deemed to be persuasive because the technical details are well known and widely used in the prior art and an artisan would be motivated to apply these techniques to a screening method simply to establish the most sensitive screening method or to screen a modulator a biologically important GPCR, e.g., melatonin 1a receptor.

Applicants argue that the Examiner has failed to supply the reason for the combination other than the hindsight obtained from the invention itself. This has been fully considered, but is not deemed to be persuasive because it is not necessary that the claimed invention be expressly suggested in any one or all of the references to justify combining their teachings; rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art *In re Keller,* 642 F.2d 413, 288 USPQ 871 9ccpa 1981).

Applicants argue that in rejecting the pending claims for obviousness the Examiner has relied on no less than eight references. This is inaccurate. Claims 1-4, 11, 14, 16, 17, 35, and 38 are rejected under 35 U.S.C. 103(a) based upon combined teachings of two cited prior art. In fact, none of the claims is rejected using more than four references.

At the 2nd paragraph of page 15 of Applicants' reply filed on 05/22/2206, Applicants conclude their argument and submit that none of the cited references, considered alone or in any combination, teaches or suggests all of the elements of Applicants' claimed invention. This is not found to be persuasive for the reasons set forth above.

Claim Objections

Claims 7, 8, 12, 13, 15, 21, 22, 26-34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

Ruixiang Li, Ph.D.
Primary Examiner
July 25, 2006

RUIXIANG LI, PH.D.
PRIMARY EXAMINER